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OFFICE ACTION

Patent Application No.

TOKUGAN No. 2004-318056

Date of drafting

November 8, 2007

Examiner of the Patent Office

Nobuyo Kamijou 9454 4C00

Patent Applicant Agent

Mr. Shunichiro Suzuki (and three others)

Applied Provisions

Article 29 Paragraph 2

This patent application should be rejected on the following grounds. In case of disagreement with this office

action, the applicant can submit a written statement within 60 days from the date of dispatching of this office action.

GROUNDS

1. The inventions relating to the following Claims of the present patent application are not patentable under the provisions of Article 29, Paragraph 2 of the Patent Law, because they are the inventions which would have been invented easily by those skilled in the art to which the present inventions belong, before the filing of the present patent application, based on the inventions described in the following publications distributed in Japan or in the foreign countries before the filing of the present patent application or on the inventions available to the public through electric communication lines.

DESCRIPTION (For cited references, see the List of Cited References)

[Ground 1]

- Claims 1 - 4
- Cited References 1 - 5
- Remarks

Cited References 1 and 2 disclose X-ray contrast medium containing liposomes having therein water-soluble and nonionic iodine-based compound such as metrixamide and iodixanol, and these liposomes are recognized not to contain chlorine-based solvent substantially, because the solvent is caused to evaporate even they are manufactured by using chloroform. It is further described that a liposome described in Cited References 2 is a single membrane.

When the inventions relating to Claims 1 - 4 of the present patent application are compared with descriptions in Cited References 1 and 2, they are different each other on the point that, in the inventions relating to Claims 1 - 4 of the present

patent application, liposomes are those formed by mixing phospholipid with supercritical carbon dioxide or with sub-critical carbon dioxide and by bringing water-soluble and nonionic iodine-based compound into contact with phospholipid, without using chlorine-based solvent, and further those wherein at lease 80% of them is occupied by a single membrane liposome, while, in Cited References 1 and 2, there is no description about manufacturing liposomes by using supercritical carbon dioxide or sub-critical carbon dioxide.

The different point mentioned above will be studied as follows.

Cited References 3 - 5 disclose a method of manufacturing a liposome in which sealed substances are capsuled, by mixing phospholipid with supercritical carbon dioxide or with sub-critical carbon dioxide and by adding aqueous phase including capsuled substances, and the aforesaid Cited References disclose that this method makes it possible to manufacture a single membrane liposome having high holding

efficiency or a multi-layer liposome, residual organic matters are not toxic because organic solvent toxic for human body is not used, and an average grain size of the liposome is reduced depending on its adjusted pressure, and it can be miniaturized to 200 nm under the adjusted pressure of 30 atmosphere.

In the aforesaid technical field, it is common that those skilled in the art select and determine a manufacturing method and a form of drug of formulas to be used specifically.

Under the foregoing, it is considered that those skilled in the art can achieve the inventions relating to the present patent application easily, by preparing liposome formed by using a liposome manufacturing method described in Cited References 3 – 5 requiring no use of highly toxic chlorine-based solvent, in medicine formula described in Cited References 1 and 2, then, by mixing phospholipid with supercritical carbon dioxide or with sub-critical carbon dioxide, and by causing water-soluble and nonionic iodine-based compound to contact with the phospholipid, or by preparing liposome in which at

least 80% is occupied by single membrane liposome, and by confirming an effect of the liposome.

Meanwhile, even when examining the description in the detailed explanation of the invention, it is impossible to recognize that the inventions relating to Claims 1 - 4 of the present patent application exhibit remarkable effects which cannot be estimated from items described in Cited References 1 - 5.

- Claims 5 - 20
- Cited References 1 - 17
- Remarks

As described in Cited References 6 - 12, causing liposomes to be modified to be PEG, and causing a compound having a polyalkylene oxide group in a lipid membrane, sterols, polyalkylene oxide modified phospholipid, and a block copolymer of polyethylene oxide and polypropylene oxide to be contained are conducted generally, for the purpose of stabilizing

liposomes, and further, when manufacturing liposomes, water-soluble amine-based buffer such as trometamol and drug product aids such as chelating agents are components to be blended commonly.

Further, as described in Cited References 2, 13 - 17, causing liposomes to be transmitted through a filter membrane for adjusting a grain size when manufacturing liposome drug product, is generally conducted.

In the present technical field, an average grain size of liposomes, types of additives, a rate of compounding and manufacturing conditions are those which can be selected and determined properly by those skilled in the art in accordance with purposes, and selection of them in the inventions of Claims 5 - 20 is not considered to have specific meaning, in view of the description of the specifications.

Further, effects of the inventions relating to Claims 5 - 20 of the present patent application cannot be considered to be remarkable ones which cannot be estimated from items

described in Cited References 1 - 17.

List of Cited References

1. Biochimica et Biophysica Acta, 1983, Vol. 756, No. 1, p. 106-110

2. Tokkaihei No. 07-316079

3. International Publication No. 02/32564

4. Tokkai No. 2003-119120

5. PHARM TECH JAPAN, April 1, 2003, Vol. 19. No. 5, p. 91-100

6. Tokkaihei No. 01-249717

7. Tokkaihei No. 06-080560

8. Tokkaihei No. 05-245357

9. Tokkaihei No. 09-003093

10. Tokkaihei No. 07-165770

11. Tokkai No. 2002-37883

12. Tokuhyo No. 2000-504334

13. Tokuhyohei No. 2-500192

14. Tokuhyohei No. 1-501228

15. Tokuhyohei No. 6-501646

16. Tokuhyosho No. 61-502452

17. Tokuhyo No. 2001-521486

(Note) Due to limits such as laws and contracts, there may be an occasion wherein a part or the whole of a non-patent document presented is not forwarded.

Record of the results of the search for prior art documents

- Searched field IPC A61K49/04
  A61K9/00-72
  A61K47/00-48
- DB name CAPLUS (STN)
  MEDLINE (STN)
  BIOSIS (DIALOG)

These records of the results of the search for prior art documents do not constitute the reasons for refusal.

<Where to call for contents of this office action>

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